State-of-the-Art

Data Ranges in Aquatic Toxicity of Chemicals

Consequences for Environmental Risk Analysis

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Abstract. A significant problem for effect assessment of aquatic ecosystems arises from the large ranges of toxicity data, which can be found in different databases and literature. Here, ranges are given for the aquatic toxicity of 27 high production volume chemicals. Based on these illustrative examples and on the current literature on uncertainty in aquatic effect assessment, toxicity ranges are discussed for their possible causes (variation in experimental condition, species, endpoint, time) and ways to handle them (safety factors). Implications and recommendations on the procedure of risk analysis of chemical substances are drawn.
Two main requirements for a comprehensive risk assessment are identified, which often play a minor role in current practice (as they are often neglected) as well as in scientific discussion (as they are meant to be trivial). **First**, data quality must be checked critically before applying any result of a toxicity test. **Secondly**, experimental data should take into account different species and acute as well as chronic data. If these aspects are considered in risk analysis, which is common practice in ecotoxicology but not always in the context of practical applications in risk engineering, a more comprehensive picture of the environmental toxicity of a chemical substance can be obtained.

Keywords: Aquatic toxicity, data range, ecological risk assessment, effect assessment, uncertainty

1 Introduction

The risk posed on aquatic ecosystems by man-made substances is an important part of all environmental risk analysis methods proposed by legal or scientific bodies. In the effect analysis as part of the environmental assessment, it is tried to estimate a concentration which has no undesired effects on the aquatic ecosystem. No Effect Levels (NEL), No Observed Effect Concentrations (NOEC), Predicted No Effect Concentrations (PNEC) or aquatic quality criteria are examples of such concentrations. The aquatic effect assessment in environmental risk analysis is usually based on a set of toxicity data obtained from environmental databases, published toxicological studies or a set of values directly measured in toxicological experiments.

Almost all toxicity data are based on laboratory tests. As these tests have been highly standardized [1], the experimental conditions for each toxicological endpoint and species are clearly defined based on Good Laboratory Practices (GLP). The effects observed at different concentrations are interpreted using a statistical model to obtain the toxic concentration for the endpoint. These statistical models and their implications on the results of the study are reviewed by Chapman et al. [2]. The experimental results obtained are published in a toxicological report or included in some kind of database. Because of this standardization, results of toxicity tests are usually well documented in toxicological studies. However, documentation decreases largely as soon as secondary information sources are considered. Many environmental databases do not include background information about the test conditions such as exact description of the endpoint, pH of exposure water, etc. The quality of documentation of toxicity data in material safety data sheets (MSDS) is even worse, although MSDS are an important data source for environmental risk assessment in industrial practice. Such background information about the exact test conditions, however, is essential for interpreting the results, as all toxicity data have to be questioned critically before being applied in risk analysis.

A major problem often encountered during risk assessment is the lack of ecotoxicological data covering key species in ecosystems. This holds in particular for chronic toxicity data. This problem of uncertainty because of missing information is addressed by estimating toxicity data via QSAR methods [3] or by estimating safe concentrations using safety factors (uncertainty factors). Most international bodies issued guidelines on which factors to apply in order to account for the different sources of uncertainty [4]. The scientific community is discussing these factors [5,6] intensively.

In the case of chemicals where a sufficient set of toxicity data exists, one major problem of aquatic effect assessment is the large range of data for the same chemical substance. Toxic concentrations can vary by several orders of magnitude depending on experimental conditions, species, endpoint, exposure time (acute – chronic) and aquatic test environment (laboratory – field). Several studies are available reporting ranges of aquatic toxicity data. Especially the difference between acute and chronic data has been studied intensively for a broad field of substances [7]. Other studies

report the range of aquatic toxicity for a specific group of chemicals especially insecticides and herbicides [8,9]. For commodity chemicals produced at high volumes, however, illustrative examples for the ranges of aquatic toxicity data are missing. This is somehow astonishing as a sufficient amount of data exists and as these substances (for instance solvents) play an important role in every-day risk assessment.

If a sufficient amount of reliable and well-documented data is available to the environmental risk manager, the toxicity ranges can be considered and the "safe" concentration for protecting ecosystems can be estimated. Detailed guidelines for aquatic risk assessment are available at many international bodies in order to simplify and harmonize the methods. These guidelines should provide every user, not only "experts" in ecotoxicology knowing the theoretical background of aquatic toxicology, with an easy-to-use "manual" on how to perform environmental risk assessment. However, there is no consensus on a scientifically and politically accepted framework for aquatic effect assessment. Especially the concept of using NOEL values for estimating "safe" concentrations has been criticized [10,11,12,13] and effect concentration at low effect levels (EC5, ...) were proposed as alternatives. Despite all guidelines, collection and interpretation of toxicity data still requires time and background knowledge in order to avoid misinterpretation. As the time available for performing a rigorous study on environmental risk is decreasing continuously at today's economic situation, practitioners are faced with the problem of not having enough time for a comprehensive literature search for the aquatic toxicity of a substance.

Despite all problems of missing data, poor data quality, large toxicity ranges and methodological discussions, practitioners sometimes believe effect assessment to be possible by simply selecting a few single values for the aquatic toxicity of a substance according to published guidelines without any toxicological background knowledge. This would largely simplify and speed-up the risk analysis process, but can lead to misinterpretations and wrong results. Similar practical problems and misunderstandings are described in the literature [14].

The goal of this study is to highlight the problems associated with the application of aquatic toxicity data in risk analysis by giving illustrative examples of 27 selected bulk chemicals. We want to show that in effect assessment, the aquatic toxicity of a compound should be based on a concentration range instead of one or a few single values. After analyzing the different reasons for the toxicity ranges, we discuss the current concept of safety factors with respect to the aquatic toxicity of the selected substances. Some recommendations are given, pleading for a critical use of a full set of data when assessing the toxicity of a chemical substance to aquatic ecosystems.

2 Methods

In order to obtain a comprehensive picture of the problems in applying aquatic toxicity data in environmental risk analysis, 27 substances of different chemical classes were selected. Their aquatic toxicity data were presented graphically for different species and endpoints.

The basis for selection was a list of High Production Volume Chemicals in the U.S. (production volume > 50,000 t) which contains many important bulk chemicals. The substances were selected, when a sufficient number of toxicity data was available in public databases (at least ten acute values and two chronic values). As an additional criterion, the selected substances should play an important role in fine chemical industry (such as solvents) and they should cover different chemical substance classes. Inorganic acids and bases were not considered, as their toxic effect is usually based on the pH change. The selected 27 substances are listed for each class in **Table 1** (note that substances can be mentioned more than once). Most substances exert their toxic effect through narcosis and membrane toxicity and act by an unspecific mode of action. Only some of them have other and specific mechanisms of toxicity such as the cyanides.

Data for the aquatic toxicity of the chemicals were taken from two different databases. ECDIN (Existing Chemicals Data Information Network – http://ecdin.etomep.net/) is a publicly available database of the European Community and includes all substances of the EINECS (European Inventory of Existing Chemical Substances) with varying amounts of data. The toxicological information was selected from primary literature by experts. ECDIN has not been kept up to date for a few years, as a new database system, IUCLID (International Uniform Chemical Information Database), is

Table 1: Selected substances

Substance class	Substance
Aliphatic hydrocarbon	Hexane
Halogenated compound	Methylene chloride, p-chlorophenol, dimethylethylhexadecylammoniumbromide
Ether	Diethylether, tetrahydrofuran
Alcohol, phenol	Methanol, ethanol, isopropanol, phenol, p-chlorophenol
Aldehyde, ketone	Formaldehyde, dimethylformamide, acetone
Acid and derivatives	Oleic acid, hydrogen cyanide, ethylacetate, acrylonitrile
Amine	Ammonia, diethanolamine, pyridin, dimethylethylhexadecylammoniumbromide
Long chain compound	Oleic acid, dimethylethylhexadecylammoniumbromide
Aromatic compound	Phenol, toluene, p-chlorophenol
Salt	$NaNO_2$, NaBr, NaOCl, $NiCl_2$, $(NH_4)_2SO_4$, NaCN

being developed. The second database used in this study is the IGS-database (Informationssystem Gefährliche Stoffe) built by Swiss Authorities (Nationale Alarm Zentrale, http://www.aac.ch/IGS/root.htm). It contains toxicity data from different other sources (databases) which were selected without further quality control.

For each substance, all toxicity data were exported from the external databases and saved as a text file. After creating a new database (Microsoft Access), all data files were imported. In a first set of calculations, the data were transformed into a standardized format (SI-units, endpoint categories according to chapter 2.1). Secondly, the following quality criteria were applied on the data:

1. Data were rejected if no information about species or endpoint was available or if no result was given (10% of data).
2. In a few cases, concentration ranges were given instead of single values. If the range exceeded the factor of 5, data were not used (e.g. effect concentration (growth, 40% increase) of toluene to alga: 0.1-10 mg/l). In the case of smaller ranges, the lower value was used (precautionary principle).

It was not possible to apply additional quality criteria, as the documentation of some data was incomplete (see chapter 4.1).

2.1 Definition of endpoint categories

Five different endpoint categories were used in this study in order to simplify the graphical representation (LC50, Effect, Chronic, LOEL, NOEL). These categories are based on toxicological endpoints but some of them are defined slightly different. "LC50" contains all acute LC50 values. The category "LOEL" includes all endpoints where a lowest concentration causing toxic effects was described. Therefore, not only Lowest Observed Effect Concentrations according to the toxicological definition were included, but also values extrapolated from a dose response relationship (e.g. EC5). The following endpoint descriptions were collected in the category "LOEL": EC5, EC10, LC5, LC10 (EC: effect concentration, LC: lethal concentration, number refers to percentage of total effect 100%), LOEL, threshold level. Similarly, the category "NOEL" is used to show all endpoints which in the data source were mentioned as EC0, LC0, no effects, NEL (No Effect Level), NOEL or NOAEL (No Observed Adverse Effect Level). This exceeds the toxicological definition of a NOEL.

All endpoints not included so far were summarized in the categories "Effect" and "Chronic". If a chronic endpoint could be identified, the category "Chronic" was applied. All remaining acute data or data without sufficient information about the time of the experiment were collected in the "Effect" category. If a LC50 value (e.g. 28 days in fish) was reported, it is shown as "Chronic" and not as "LC50" value in all graphs. All acute lethal concentrations besides the LC50 values (such as LC100, LC25, total mortality) are presented in the category "Effect".

This classification results in one narrowly defined endpoint category ("LC50") and four broad categories summarizing similar endpoints. All data were graphically presented using these categories.

3 Results

3.1 Experimental parameters influencing toxicity

The exact experimental conditions are of highest importance for obtaining comparable results in toxicological studies. For acrylonitrile, the time course of toxicity is shown in **Fig. 1**. The LC50 / EC50 values for *Leuciscus idus* decrease for 2-3 orders of magnitude when comparing values for 1 and 96 hours. This is a well-known fact of the toxicological response of organisms and only the 96h value will be used in effect assessment. However, if the time information is not included in the data-source, these two values can not be distinguished and the variability of toxicity results can not be explained.

An experiment for measuring the aquatic toxicity of a given substance can be designed as static or flow-through test depending on the mode of adding and controlling the tested substance. As soon as volatile, degradable or adsorbable substances are tested, this can lead to large ranges in results. Fig. 2 illustrates this problem using the highly volatile acetone as example. Toxicity data for *Daphnia magna* are lower

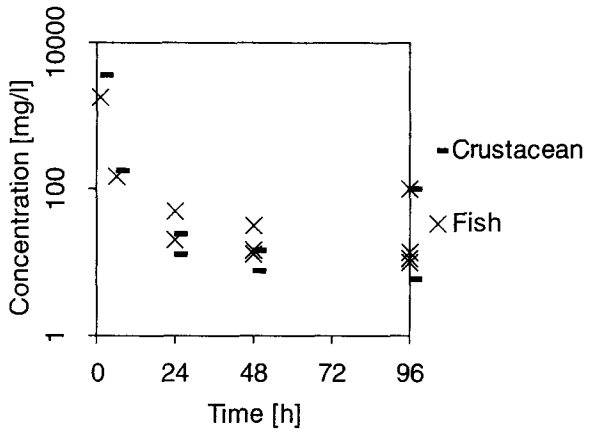

Fig. 1: Influence of time on LC50 / EC50 values of acrylonitrile

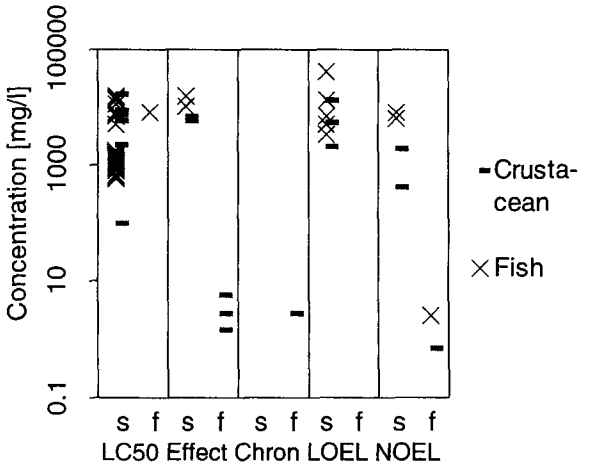

Fig. 2: Influence of water flow on toxicity of acetone. s: static, f: flowthrough

by a factor of 1000, if flow-through tests are compared to static experiments. As acetone evaporates, the effective concentration can largely decrease during static experiments. In flow-through tests, acetone is added throughout the experiment to keep a constant concentration. Therefore a much higher amount of acetone added at the beginning was required in the static test to reach equal toxic effects as in flow-through experiments.

Similar differences in toxicity data can be caused by differences in the pH-value of the experiment, if protonable or deprotonable substances are tested.

3.2 Comparison within related species

Aquatic toxicity strongly depends on the animal or plant species under consideration. As an example, the toxicity of toluene for different fish species is shown in Fig. 3. Between the different species, the LC50 values vary by the factor of 200 (interspecies variability). Within one species (intraspecies variability) the range is smaller and does not exceed a factor of 10. Effect-concentrations exhibit higher ranges (factor of 5,000). This fact can mainly be contributed to differences in the measured effect (*Cyprinus*: blood serum concentration; *Leuciscus*: letal effects; other fish species: behavior, reproduction). Toluene as an example corresponds quite well with the ranges of intraspecies variability which generally is reported not to exceed a factor of 10 for most substances [5].

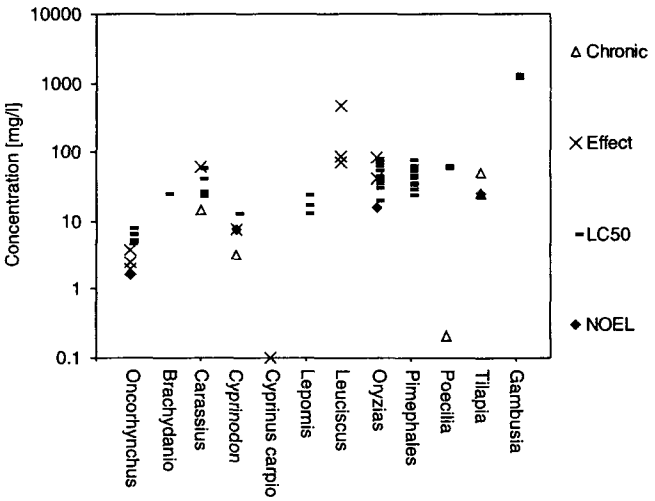

Fig. 3: Intra- and interspecies variability in toxicity of toluene to different fish species

3.3 Comparison of different species

To illustrate the species differences, the aquatic toxicity of diethanolamine is shown in Fig. 4 as a representative example. Similar graphs were built for all 27 substances but are not shown here. Diethanolamine is known to be toxic to liver and kidney of higher vertebrates. At the cellular level it leads to changes in the phospholipids of the cell membranes [15]. Some carcinogenic effects are reported as well, as nitrosamines can be formed during metabolism [15]. LC50 values range between 20 and 5,000 mg/l. The ranges within fishes and crustacean span a factor of about 10. For one alga, *Skeletonema costatum*, the toxic concentration lies two orders of magnitude below that of other algae species (*Scenedesmus, Selenastrum*) (*see* chronic and NOEL values of *Fig. 4*). High interspecies variabilities and high sensitivities have been reported for algae also for other compounds [16]. Crustaceans and algae are the most sensitive species for diethanolamine, whereas fishes are a factor of 100 less sensitive. If only fish data were used for an effect assessment, the risk would largely be underestimated even if a safety factor of 10 were used.

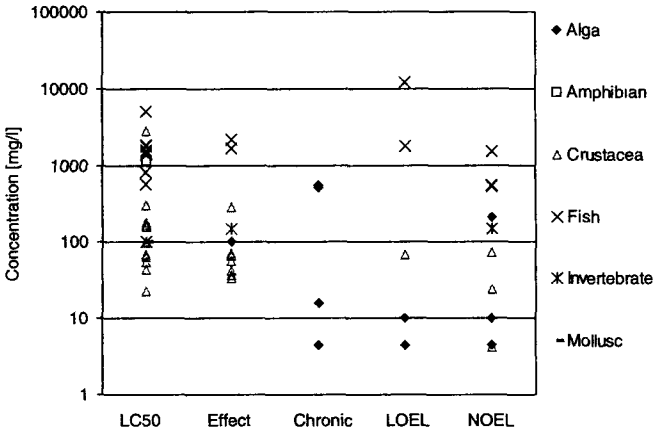

Fig. 4: Aquatic toxicity of diethanolamine

3.4 Comparison of different substances

Fig. 5 (→ *p. 139*)gives an overview of the acute aquatic toxicity of all 27 substances (without NOEL and LOEL values). All substances are roughly ordered by decreasing polarity starting with salts at the left-hand side and ending with hexane on the right. On first sight, the large ranges of aquatic toxicity can be seen which cover two to four orders of magnitude for most substances. Higher variabilities (factor of 100,000) can be observed for NaOCl, formaldehyde, acetone, dimethylformamide and methanol. Some single values at the higher end of the concentration range can be explained with inadequate experimental design (static tests: ammonia, NaOCl, $NaNO_2$, acetone; short test periods: acrylonitrile). Applying more restrictive quality criteria would reduce the ranges for the mentioned substances by a factor of 10 to 100. Such strict criteria would, however, remove almost all data for some other compounds.

The largest number of toxicity data were for fish and crustaceans. Toxicity data for algae and molluscs were available for two thirds and half of the compounds, respectively. A comparison of the toxicity of the different substances to other aquatic organisms was not possible, because data were lacking for most substances. No species can be identified which is most sensitive to all substances studied, which is well known in ecotoxicology [8]. General trends of the toxicity results themselves or of the size of the overall variability could not be seen. This is not surprising as different modes of toxic action are involved.

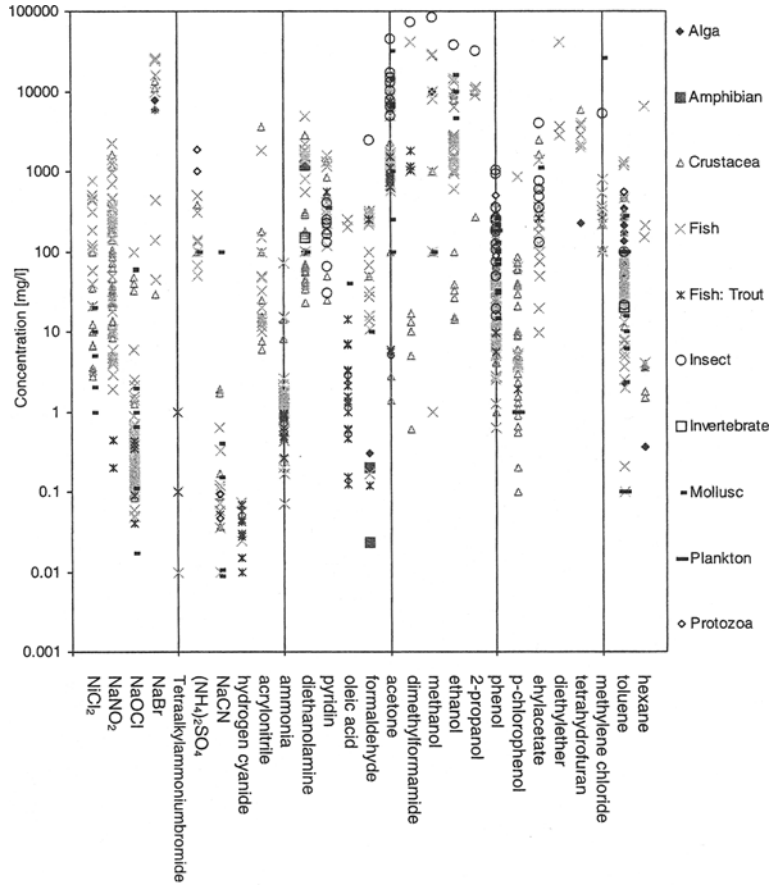

Fig. 5: Acute aquatic toxicity (LC20 – LC100, EC20- EC100) of selected substances

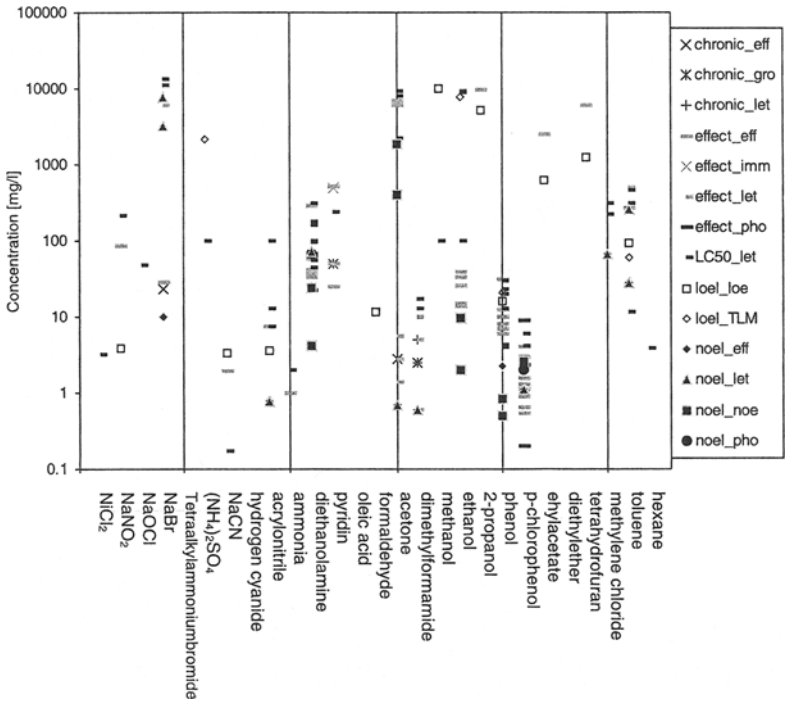

Fig. 6: Comparison of endpoints of toxicity to *Daphnia magna*. _gro: growth _let: mortality, _imm: immobilization, _pho: phototaxis, _eff: other effects, _TLM: probably threshold limit, _loe: LOEL, _noe: NOEL

3.5 Comparison of different endpoints

One major reason for ranges in toxic concentrations is the difference in the endpoint measured in the experiments. Sublethal effects usually occur at concentrations which do not cause mortality of the organism. Therefore, lethal concentrations normally have higher values than effect concentrations under comparable experimental conditions. First physiological or chemical changes in the organism can already occur at much lower concentrations, where no macroscopic effect can be observed. Therefore, the exact description of effect concentrations is essential for interpreting the results of the toxicological study.

Fig. 6 (→ *p. 139*) shows different endpoints of the toxicity to *Daphnia magna*. The data picture is not completely consistent with theory, partly because quality and quantity of the data was not high enough. NOEL values (except LC0 values) lie at the lower end of the toxic range for most substances. For p-chlorphenol, however, effect concentrations (phototaxis, enzyme inhibition) are reported below the NOEL values (factor of 10). LOEL values can not be found between effect concentration and No Effect Concentrations, but are spread over the whole range of toxicity data. This fact can be explained with the lack of clear documentation and missing of exact definition of most LOEL values. LC50 values usually are above sublethal effect concentrations by factors between 1 and 10.

4 Discussion

4.1 Quality of data

One of the main practical problems of interpreting toxicological data is that the documentation and the quality of the information often is poor, especially in broadly used data sources (such as official databases, MSDS). In this study, no strict quality criteria could be applied, such as minimum testing time, exact description of endpoint and experimental conditions (controlled pH, no static tests) and meaningful citation of data source. Especially the IGS-Data source was quite unsatisfactory in this respect, although it is the official database recommended by Swiss Authorities. The exact documentation of the experimental conditions (pH, temperature, static or flow-through, etc.) was only given for half of the results. A rough description of the endpoint (such as EC50) and species (such as fish) was available for almost all data (95%). However, an exact allocation to chronic or acute tests could only be done in 70% of the results, as for the others no testing time was given. On an additional 15%, data could be ascribed as acute values, as LC50 values commonly are acute endpoints.

In principle, an exact definition of the most common toxicological endpoints (such as NOEL, LC50, LOEL, EC50) exists. However, a large variety of descriptions and slightly different definitions exist for most endpoints in toxicological information systems. This poses problems for users willing to interpret toxicological data accordingly. In particular, databases show an astonishing and often unclear variety of endpoint descriptions (e.g. TLM, TDLo, LDLo, threshold value, normal effects, increasing mortality, etc.). In most cases, it was possible to attribute standardized endpoints to the verbal descriptions; in some other cases, however, the endpoint description (such as "acute" or "chronic") were of limited value. The danger of poor documentation of toxicity data is the tempting possibility of rejecting undesirable data because of low quality, but of accepting suitable data without critical evaluation. Critical questioning of the toxicological data used for risk assessment is a crucial point for avoiding misinterpretation during the assessment process.

Fig. 1 and 2 show how important the experimental conditions (e.g. time, water flow) are for interpreting the results. It should be emphasized that the experimental conditions must be documented for meaningful interpretation. This criterion is fulfilled for most data measured since toxicological experiments were standardized in the 80's, particularly those performed under GLP conditions. As an important quality criterion of toxicological information media such as substance datasheets or databases, the full documentation of all important experimental parameters must be included. If this information is missing, selecting a single value or using statistical methods for interpreting the results can lead to large errors. The aquatic risk can be over- or underestimated by several orders of magnitude. Additionally, the standardization of ecotoxicological endpoints should be further developed and communicated to the public. Every ecotoxicological endpoint which might not be known by all possible users of the results should be defined clearly when passing on toxicological information. This could avoid misinterpretations and misunderstandings of aquatic toxicity data.

4.2 Data ranges and concept of safety factors

Aquatic toxicity data for a substance always cover a certain concentration range. Several reasons are known for this fact such as differences within a species and between species, endpoints, replicates, exposure time, laboratories and between laboratory and field tests [8]. Using only a single or a few values can never deliver a reliable picture of all ecotoxicological effects of a substance. Thus, toxicity can be over- and underestimated by several orders of magnitude depending on substance and data quality. Only if a sufficient amount of reliable data is available covering all mentioned reasons for variability, a "safe" concentration for the aquatic ecosystem can be estimated. This condition, however, is fulfilled for only a very small number of substances due to different (especially economic) reasons. Usually, only a much smaller number of data which is at the fingertip of the user will be applied. As only some of the ranges can be covered, the remaining uncertainty of missing information has to be dealt with before estimating the "safe" concentration. A similar problem arises when substances with different levels of information about toxicity are compared. Detailed aquatic toxicity data for one substance can not be used for comparison if corresponding values are missing for the other substance. To resolve these problems, the concept of safety factors (uncertainty factors) has been proposed.

If no chronic or sublethal effect data, or no NOEL values or field studies are available, the use of safety factors has been recommended for extrapolating "safe" concentrations from LC50 values [4]. These factors are based both on policy and

science and try to estimate concentrations that are very probably lying below the real values. The goal of safety factors is to keep the probability of underestimating the risk low, independently of the amount of toxicity data. This pragmatic concept allows effect assessment based on single LC50 values. Usually factors of 10 for extrapolation of lethal to sublethal, acute to chronic, inter- and intraspecies variability and LOEL to NOEL are proposed. A detailed discussion of these safety factors, their background and problems was done by Chapman et al. [5]. Some aspects are summarized below and discussed with respect to the results of the present study.

4.2.1 Acute-chronic ratio

Chronic toxicity tests cover a considerable part of the life span of organisms. They are quite time consuming and costly to perform and therefore attempts have been made to develop extrapolation methods to estimate chronic from acute data. The acute-chronic ratio plays an important role in legislation (e.g. water quality criteria in the U.S.) [17]. Using such ratio, the chronic quality criterion (Final Chronic Value) can be estimated from the acute criterion (Final Acute Value). The OECD guidelines propose an average factor of 10, if chronic data are missing. This factor was obtained from the 50% percentile of a study of the ratios between 96h LC50 and chronic NOEL values for 72 substances [7]. The ratios ranged from values of 0.13 to 1300, which is an indication of the problems associated with this extrapolation.

The use of a constant acute-chronic ratio for all substances has been partly supported [6], but is being increasingly criticized from an ecotoxicological point of view. The extrapolation from acute to chronic toxicity is based on statistical analysis rather than toxicological concepts. In the past, a factor of 10 seemed to be sufficiently protective for most substances and species, as chronic data were quite rare. During the last decade, a number of examples have been reported [5,8], where the ratio between acute and chronic data can not be represented with a constant factor of 10. First, the ratio strongly depends on the species and substance, and second, it can reach much higher values (>1000). This fact is not surprising, as different toxicological mechanisms can be responsible for chronic and acute toxicity. For the 27 substances in this study, conclusions for the acute-chronic ratio could not be drawn, as not enough chronic data of sufficient quality were available.

As this extrapolation is scientifically questionable, it is essential to use chronic data from experiments or substance-specific estimation methods for aquatic effect analysis. The general safety factors for acute-to-chronic extrapolation can neither predict chronic toxicity, nor assure the protection of aquatic ecosystem when trying to extrapolate "safe" concentrations.

4.2.2 Inter- and Intraspecies variability

Considering the enormous evolutionary diversity of aquatic species, it can be easily understood that different sensitivities exist for the same substance. Evolutional, biological, physiological-morphological and ecological differences between organisms are among the reasons for this diversity. Some earlier studies [18] reported ranges of a factor of 2-50 for LC50 values, whereas in recent studies [5,8] much larger ranges (>10,000) were reported. Similar high ranges of several orders of magnitude can be seen in **Fig. 5**. A statistical evaluation yielding mean and maximal variability strongly depends on the quality criteria applied on the raw data and would therefore not give any additional information. Even within closely related species, a high variability of a factor of 10,000 was shown for some specific substances such as organophosphate pesticides (e.g. disulfoton) [8]. These large ranges are desired as the substances are designed to exhibit high selectivity on a specific group of organisms. For most substances, however, aquatic toxicity to similar species does not exceed a range of 10 to 100, especially since detailed guidelines for conducting toxicological experiments are being followed.

From the practical point of view, it would be desirable in risk assessment to identify a most-sensitive species, from which extrapolation to all other species would be possible. This would largely simplify risk assessment of new substances, as only one species would have to be tested and the resulting concentration would protect all species. However, such most sensitive species does not exist for several reasons. This can be seen in **Fig. 5**. If crustaceans were assumed to be the most sensitive species, the lowest toxic concentrations would be found for 45% of the substances considered in this study. For 20% of the substances, other species are more sensitive by a factor >100. Applying a safety factor of 10 would not be sufficient for these substances. Thus, for assessing aquatic effects it is essential to have data for several species of different phyla and trophic levels [8,14].

4.2.3 Extrapolation to different endpoints

Fig. 6 compares different endpoints. General correlations allowing extrapolation from one endpoint to another (such as lethal to sublethal effects, LOEL to NOEL) could not be observed. Such constant extrapolation factors can be defined with statistical means for ideal data, i.e. data measured in the same laboratory with the same organisms under exactly the same experimental conditions. Applying them on real data from different sources with partly unknown quality can result in large errors and unrealistic values. If such safety factors are used for aquatic effect assessment, the risk can be overestimated by several orders of magnitude. Especially, the aggregation of a number of factors often leads to unrealistically low values [19]. If NOEL values were extrapolated for the studied substances applying extrapolation factors on LC50 / EC50 values, the results would be lower by a factor between 1 and 1000 than the real NOEL values. Thus, the current system of endpoint extrapolation estimates values, which are protective but often unrealistically low. One exception might be the safety factor of 10 proposed by the European Union to extrapolate from a LOEL to a NOEL for human effect assessment [4]. It can only be applied if the quality of the LOEL is without any doubt. Otherwise this extrapolation might underestimate the risk.

General extrapolation factors must not be used to predict toxicity data for other endpoints. For comparison of the

aquatic toxicity of two substances (one with a full data set, one with little data), there is no advantage in using any of those factors. From a legal point of view, it is possible to close data gaps using such factors, as they estimate more or less "safe" concentrations in order to protect the environment. From a scientific point of view, the use of general extrapolation factors for predicting aquatic toxicity is questionable.

4.3 NOEL / LOEL concept in risk analysis

Most existing concepts of risk analysis rely on the No Effect Level (NEL), which is the real concentration not causing any undesired effects in the aquatic environment. This is a hypothetical value, which can not be measured experimentally. Therefore, a NOEL is commonly used to estimate the NEL. In the last decade this concept of NOEL has been criticized [2,10,11,12,13] for the following reasons.

A NOEL is obtained as the highest experimentally measured concentration, where no significantly different effects were observed between the test group and the control group of the experiment. The significant difference is analyzed using one of the statistic hypothesis test procedures usually with a significance interval of 5%. Laskowski showed that this significance level often does not correspond to the desired error probability of underestimating the aquatic risk [13]. The error probability of obtaining a (wrong) concentration as result (i.e. as the NOEL), at which toxic effects still occur but simply have not been detected because of pure chance, usually is between 10 and 20% or even higher [13].

Chapman et al. [10] showed different examples of how the choice of data interpretation method (hypothesis test) can influence the result of the study (i.e. the NOEL) using the same experimental data. Similarly, a different choice of concentrations used in toxicity experiments can lead to large differences in the resulting NOEL. The main reason for this problem of the NOEL concept is that only one single value of the whole experiment is used for obtaining the result instead of the whole dose-response curve. A small change in experimental data which, for instance, increases the error probability from 4.9 to 5.1% finally leads to a large change in the NOEL, because the next measured (lower) concentration has to be used. This can be the reason why the ranges for NOEL values are reported to be higher than for EC50 values [10].

Several alternatives were proposed instead of the NOEL concept using different kinds of effect concentrations (from EC50 down to EC0) [2,10,11]. Problems of hypothesis test selection, dependence on experimental conditions can be avoided by fitting a statistical distribution to all experimental data using regression analysis. From this distribution model, the desired effect level can be calculated. The kind of statistical distribution and regression analysis has no significant influence as long as it is used for interpolation between measured values. However, if a concentration at low effect levels such as EC0 or EC5 shall be extrapolated, the result largely depends on the choice of the model.

The dependence on statistical models can lead to large uncertainties for both EC0 and NOEL values. The endpoint, which has the lowest uncertainty ranges caused by statistical or experimental reasons, is the EC50 (LC50) value. For substances with similar slopes of the dose-response curves, such endpoints should be used for comparing the aquatic toxicity of different substances. The principal problem of estimating a NEL, a concentration at which no effects occur, can be improved but not completely solved by the alternative concepts to the NOEL.

We understand the criticism of the NOEL concept as one which is largely based on mathematical/statistical reasoning. Compared to the data ranges caused by the different sources of variability, these theoretical considerations have to be relativated, especially if a pragmatic approach to aquatic effect assessment is sought.

5 Conclusion

Assessing aquatic effects of chemical substances is a major task in environmental risk assessment. Although a number of guidelines exist, several problems can occur during this procedure, especially for non-experts in ecotoxicology. The first important step of successful effect assessment is to question all toxicological data critically before applying them. All background information required for this quality check must be made available in primary and also in secondary information media for toxicological data.

Ecotoxicological data always consist of a range of concentrations depending on species, endpoint, time-scale and experimental conditions. To get a comprehensive impression of the aquatic toxicity of a substance, the whole range must be considered and covered with data. This especially includes data for different species of different trophic levels and acute as well as chronic data. From the legal point of view, safety factors provide a useful and pragmatic means to deal with these uncertainties as they usually (with some exceptions) lead to "safe" concentrations which protect the environment. For predicting toxicity data in order to compare the true aquatic toxicity of two substances, general safety factors should not be used. If the quality and the ranges of toxicity data are not considered adequately, the risk in the aquatic ecosystem can be under- or overestimated by several orders of magnitude.

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